



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE

United States Patent and Trademark Office

Address: COMMISSIONER FOR PATENTS

P.O. Box 1450

Alexandria, Virginia 22313-1450

www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/560,497	12/12/2005	Lars Terje Holmaas	PN0324	4578
36335 7590 08/23/2010 GE HEALTHCARE, INC. IP DEPARTMENT 101 CARNEGIE CENTER PRINCETON, NJ 08540-6231				
EXAMINER				
KATAKAM, SUDHAKAR				
ART UNIT		PAPER NUMBER		
1621				
MAIL DATE		DELIVERY MODE		
08/23/2010		PAPER		

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE

U.S. Patent and Trademark Office

Address: COMMISSIONER FOR PATENTS

P.O. Box 1450

Alexandria, Virginia 22313-1450

www.uspto.gov

APPLICATION NO./ CONTROL NO.	FILING DATE	FIRST NAMED INVENTOR / PATENT IN REEXAMINATION	ATTORNEY DOCKET NO.
10/560,497	12/12/2005	Lars Terje Holmaas et al.	

GE HEALTHCARE, INC.
IP DEPARTMENT 101 CARNEGIE CENTER
PRINCETON, NJ 08540-6231

EXAMINER

KATAKAM, SUDHAKAR

ART UNIT	PAPER NUMBER
----------	--------------

1621

MAIL DATE	DELIVERY MODE
-----------	---------------

08/23/2010

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte LARS TERJE HOLMAAS, OLE MAGNE HOMESTAD,
JAN CERVENKA, and KHALID HUSSAIN

Appeal 2010-000515
Application 10/560,497
Technology Center 1600

Before DONALD E. ADAMS, DEMETRA J. MILLS, and MELANIE L.
McCOLLUM, *Administrative Patent Judges*.

McCOLLUM, *Administrative Patent Judge*.

DECISION ON APPEAL¹

This is an appeal under 35 U.S.C. § 134 involving claims to an
iohexol production process. The Examiner has rejected the claims as
obvious. We have jurisdiction under 35 U.S.C. § 6(b). We affirm.

¹ The two-month time period for filing an appeal or commencing a civil
action, as recited in 37 C.F.R. § 1.304, or for filing a request for rehearing,
as recited in 37 C.F.R. § 41.52, begins to run from the “MAIL DATE”
(paper delivery mode) or the “NOTIFICATION DATE” (electronic delivery
mode) shown on the PTOL-90A cover letter attached to this decision.

STATEMENT OF THE CASE

Claims 1-21 are pending and on appeal (App. Br. 1). The claims have not been argued separately and therefore stand or fall together. 37 C.F.R. § 41.37(c)(1)(vii). We will focus on claim 1, which reads as follows:

1. A process for the production of iohexol comprising alkylating 5-(acetamido)-N,N'-bis(2,3-dihydroxypropyl)-2,4,6-triiodoisophthalamide with a 2,3-dihydroxypropylating agent in the presence of a base and of a solvent which solvent comprises a C₁-C₅-monoalkylether of a C₃-C₁₀ alkylene-glycol.

Claims 1-21 stand rejected under 35 U.S.C. § 103(a) as obvious in view of Malthe-Sorensen et al. (US 5,948,940, Sep. 7, 1999) (Ans. 4).

The Examiner relies on Malthe-Sorensen for teaching “a process for the production of iohexol, said process comprising reacting 5-(acetamido)-N,N'-bis(2,3-dihydroxypropyl)-2,4,6-triiodoisophthalamide with a 2,3-dihydroxypropylating agent in the presence of a base and a solvent, viz., 2-methoxy-ethanol . . . [,] which is a C₁-C₅-monoalkylether of a C₂-C₁₀ alkylene-glycol” (Ans. 4). The Examiner concludes that it would have been obvious “to have modified the reference’s teachings by using an alternative solvent, such as 1-methoxy-2-propanol with a reasonable expectation of success” (*id.* at 5). In support of this position, the Examiner finds that the “solvents differ by one carbon” and, relying on *In re Henze*, 181 F.2d 196 (CCPA 1950), “note[s] that adjacent homologs are considered to be obvious absent unexpected results” (*id.*).

ISSUE

Does the evidence support the Examiner’s conclusion that it would have been obvious to modify the iohexol production process disclosed in Malthe-Sorensen to use a solvent comprising 1-methoxy-2-propanol?

FINDINGS OF FACT

1. The Specification discloses that “WO-A-02/083623 discloses the purification of crude iohexol using 1-methoxy-2-propanol as the solvent optionally in a mixture with other solvents” (Spec. 2).

2. Malthe-Sorensen discloses “a process for the production of iohexol . . . comprising reacting 5-acetamido-N,N'-bis(2,3-dihydroxy-propyl)-2,4,6-triodophthalamide with a 2,3-dihydroxypropylating agent in the presence of a solvent . . . compris[ing] 2-methoxy-ethanol and, optionally, isopropanol” (Malthe-Sorensen, col. 2, ll. 1-7).

3. Malthe-Sorensen also disclose that “[t]he reaction solvent preferably is 2-methoxy-ethanol; however a mixture of 2-methoxy-ethanol and isopropanol may be used, e.g. up to 95 vol % isopropanol may be used” (*id.* at col. 2, ll. 39-42).

4. Malthe-Sorensen also discloses that the process “is preferably effected in the presence of a base” (*id.* at col. 2, ll. 53-54).

5. In addition, Malthe-Sorensen discloses:

The crude iohexol obtained . . . may then be purified preferably by recrystallization.

In the method of the invention, the crude iohexol starting material . . . is first dissolved in the crystallization solvent. In one particularly preferred embodiment, the solution used may simply be the reaction mixture from the process of the invention, optionally after adjustment of its salt content, with the isopropanol/2-methoxy-ethanol content of the solvent if necessary also being adjusted.

(*Id.* at col. 3, ll. 11-22.)

6. In a Rule 132 Declaration, one of the inventors states: A different homolog, 2-ethoxyethanol, was initially considered, but “was

impossible to use . . . due to solubility and selectively. 1-methoksy-2-pronanol [sic] (PM) was not considered since it was estimated to be even less polar than 2-ethoxyethanol.” (Decl. 1.)²

7. The Rule 132 Declaration also states:

To be able to use a solvent in the alkylation step it is necessary that NaOH is soluble. . . . Regarding PM, NaOH was not soluble. . . . At first a modification of PM by adding co-solvents for increasing solubility of NaOH was not considered due to the assumption that such an addition would worsen selectivity of the reaction. This is true for 2-ME. It was therefore definitely not obvious to pursue this lead any further.

(*Id.* at 1-2.)

8. In addition, the Rule 132 Declaration states: “In summary it was not believed that PM was able to substitute 2-ME. This assumption was based on decades of experience with these processes and general chemical knowledge.” (*Id.* at 2.)

PRINCIPLES OF LAW

Obviousness analysis “need not seek out precise teachings directed to the specific subject matter of the challenged claim.” *KSR Int’l Co. v. Teleflex Inc.*, 550 U.S. 398, 418 (2007). Instead, it proper to “take account of the inferences and creative steps that a person of ordinary skill in the art would employ.” *Id.* “A person of ordinary skill is also a person of ordinary creativity, not an automaton.” *Id.* at 421.

Structural relationships may provide the requisite motivation or suggestion to modify known compounds to obtain new compounds. For example, a prior art compound may suggest

² The page citations are to the Declaration as filed on July 14, 2008, rather than the reformatted version submitted with the Appeal Brief.

its homologs because homologs often have similar properties and therefore chemists of ordinary skill would ordinarily contemplate making them to try to obtain compounds with improved properties.

In re Deuel, 51 F.3d 1552, 1558 (Fed. Cir. 1995).

“[A]ll disclosures of the prior art, including unpreferred embodiments, must be considered.” *In re Lamberti*, 545 F.2d 747, 750 (CCPA 1976).

A reference may be said to teach away when a person of ordinary skill, upon reading the reference, would be discouraged from following the path set out in the reference, or would be led in a direction divergent from the path that was taken by the applicant. The degree of teaching away will of course depend on the particular facts; in general, a reference will teach away if it suggests that the line of development flowing from the reference's disclosure is unlikely to be productive of the result sought by the applicant.

In re Gurley, 27 F.3d 551, 553 (Fed. Cir. 1994).

“An assertion of what seems to follow from common experience is just attorney argument and not the kind of factual evidence that is required to rebut a *prima facie* case of obviousness.” *In re Geisler*, 116 F.3d 1465, 1470 (Fed. Cir. 1997). However, “[i]f a *prima facie* case is made in the first instance, and if the applicant comes forward with reasonable rebuttal, whether buttressed by experiment, prior art references, or argument, the entire merits of the matter are to be reweighed.” *In re Hedges*, 783 F.2d 1038, 1039 (Fed. Cir. 1986). “Appellant's opinion on the ultimate legal issue is not evidence in the case. . . . [However,] some weight ought to be given to a persuasively supported statement of one skilled in the art on what was not obvious to him.” *In re Lindell*, 385 F.2d 453, 456 (CCPA 1967).

ANALYSIS

Malthe-Sorensen discloses “a process for the production of iohexol . . . comprising reacting 5-acetamido-N,N'-bis(2,3-dihydroxy-propyl)-2,4,6-triiodophthalamide with a 2,3-dihydroxypropylating agent in the presence of a solvent . . . compris[ing] 2-methoxy-ethanol” and a base (Findings of Fact (FF) 2 & 4). We agree with the Examiner that it would have been *prima facie* obvious to replace 2-methoxy-ethanol with an adjacent homolog, 1-methoxy-2-propanol.

Appellants argue, however, that Malthe-Sorensen “does not teach, describe, or suggest using any other solvent other than 2-methoxy-ethanol” (App. Br. 3). We are not persuaded. Instead, we agree with the Examiner that the structural relationship between 2-methoxy-ethanol and 1-methoxy-2-propanol provides the suggestion to use 1-methoxy-2-propanol rather than 2-methoxy-ethanol. *See In re Deuel, supra*.

Appellants also argue:

[I]t was known from WO02/083623, as discussed in the present specification, page 2, lines 1-2, to use 1-methoxy-2-propanol as solvent in the purification by recrystallization of iohexol.

The fact that a solvent is known for its use as the dominant solvent in the crystallisation step of the same process would clearly teach away from using the same in the alkylation step.

(App. Br. 4.) We are not persuaded.

Claim 1 requires that the solvent *comprise* a C₁-C₅-monoalkylether of a C₃-C₁₀ alkylene-glycol. It does not exclude the presence of a co-solvent, as taught by Malthe-Sorensen (FF 2-3), or even require that the predominant solvent is a C₁-C₅-monoalkylether of a C₃-C₁₀ alkylene-glycol. In addition, as recognized by Appellants, Malthe-Sorensen describes “using 2-methoxy-

ethanol as a solvent in both the alkylation and in the purification step” (App. Br. 5; *see also* FF 2 & 5). We also note that Appellants’ argument is based on attorney argument and “not the kind of factual evidence that is required to rebut a *prima facie* case of obviousness.” *In re Geisler, supra*. Thus, we cannot agree that the evidence of record teaches away from using the same solvent in both steps.

In addition, Appellants argue that the Declaration of one of the inventors demonstrates that using 1-methoxy-2-propanol would not have been obvious (App. Br. 5-6). We are not persuaded.

The Declaration states that “it was not believed that [1-methoxy-2-propanol] was able to substitute [2-methoxy-ethanol]” (FF 8). In addition, the Declaration provides reasons for this belief (FF 6-7). However, on balance, we do not agree that this evidence is sufficient to demonstrate that one of ordinary skill in the art would not have found it obvious to replace, in the production of iohexol, 2-methoxy-ethanol, which was known to be used as a solvent in both the production and purification of iohexol (FF 2 & 5), with an adjacent homolog thereof, 1-methoxy-2-propanol, which was known to be used as a solvent in the purification of iohexol (FF 1). In this regard, we note that, contrary to the indication in the Declaration that Appellants did not consider adding co-solvents “due to the assumption that such an addition would worsen selectivity of the reaction” (FF 7), Malthe-Sorensen specifically discloses the use of a co-solvent in the production of iohexol (FF 2-3), albeit in a non-preferred embodiment. However, “all disclosures of the prior art, including unpreferred embodiments, must be considered.” *In re Lamberti, supra*.

CONCLUSION

The evidence supports the Examiner's conclusion that it would have been obvious to modify the iohexol production process disclosed in Malthe-Sorensen to use a solvent comprising 1-methoxy-2-propanol.

TIME PERIOD FOR RESPONSE

No time period for taking any subsequent action in connection with this appeal may be extended under 37 C.F.R. § 1.136(a).

AFFIRMED

cdc

GE HEALTHCARE, INC.
IP DEPARTMENT 101 CARNEGIE CENTER
PRINCETON, NJ 08540-6231